

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

## Hydroboration. XIX. The Reaction of Diisopinocampheylborane with Representative *trans* and Hindered Olefins. Triisopinocampheylborane as a Reagent for the Configurational Assignment of Alcohols and Olefins *via* Hydroboration

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In contrast to the fast, highly stereoselective reactions of diisopinocampheylborane with reactive *cis*-olefins, the corresponding reactions of this reagent with *trans* and hindered olefins are slow, proceeding only with the displacement of  $\alpha$ -pinene from the reagent, and the oxidized products exhibit much lower optical activities—13 to 22%, instead of the 70 to 90% realized with the *cis*-olefins. Moreover, the rotations of the products are the opposite to those observed in the products obtained from the *cis*-olefins or predicted from the model previously proposed. The fact that the reaction proceeds only with the displacement of  $\alpha$ -pinene indicates that the hydroborating agent is triisopinocampheylborane, formed by the concurrent dissociation of *sym*-tetraisopinocampheylborane (diisopinocampheylborane dimer). Triisopinocampheylborane was prepared and used to hydroborate some representative hindered olefins. The reaction proved to be relatively fast and yielded results similar to those realized previously in the slow reaction with diisopinocampheylborane. In spite of the modest rotations exhibited by the products, the observed configurations proved to be consistent, suggesting that the reaction should be useful as an empirical method for establishing the configuration of optically active alcohols and olefins realized *via* application of the hydroboration reaction to *trans* and hindered olefins. This conclusion was tested by converting 1-methylcyclopentene into optically active (*-*)-*trans*-2-methylcyclopentanol. The predicted configuration of the product, 1*R*:2*R*, was confirmed by transformation of the alcohol into (+)-3-methylcyclopentene of known configuration. Consequently, both diisopinocampheylborane and especially triisopinocampheylborane should be valuable as a means of converting *trans* and hindered olefins into products of moderate optical activity (~13 to 22%) and for the establishment of their absolute configurations.

The hydroboration of *cis*-olefins with optically active diisopinocampheylborane provides a convenient method for the synthesis of alcohols in high optical purity.<sup>2,3</sup> Moreover, the reagent permits the partial resolution of racemic olefins.<sup>3,4</sup> Finally, the configurations of the optically active alcohols and olefins obtained can be deduced on the basis of a steric model proposed for the reaction path.<sup>3,5</sup>

Preliminary experiments indicated that the hydroboration of *trans* and hindered olefins with diisopinocampheylborane proceeds quite slowly, with  $\alpha$ -pinene becoming displaced from the reagent as the reaction proceeds. The alcohols realized on oxidation of the hydroboration product exhibited only a modest optical purity (13 to 22%). Moreover, their absolute configurations did not conform to predictions based on the model which served so well for the *cis*-olefins.<sup>3,5</sup>

In view of these observations, a detailed study was undertaken on the reaction of diisopinocampheylborane with representative *trans* and hindered olefins. In the course of the investigation it became evident that the active hydroborating agent in these reactions must be triisopinocampheylborane and the study was extended to this reagent.

### Results

**Reaction of *trans*-Olefins with Diisopinocampheylborane.**—The reaction of *cis*-2-butene with (+)-diisopinocampheylborane at 0° is essentially complete within 2 hr. Oxidation of the product produces (+)-2-butanol of 86 to 87% optical purity.<sup>2,3</sup> In contrast, the reaction of *trans*-2-butene with the reagent under the same conditions was only 46% complete in 13 hr., and was essentially complete only after 24 hr. Oxidation yielded (*-*)-2-butanol,  $[\alpha]_D -1.75^\circ$ , indicating an optical purity of 13%.<sup>6</sup>

In the course of isolating the 2-butanol, the presence of a significant quantity of  $\alpha$ -pinene was indicated. Gas chromatographic analysis revealed the presence of 11.6 mmoles of  $\alpha$ -pinene after 13 hr., as compared

to 23 mmoles of *trans*-2-butene utilized, and 24.6 mmoles of  $\alpha$ -pinene at the completion of the reaction (24 hr.), corresponding to 50 mmoles of *trans*-2-butene reacted. These results indicate that 1 mole of  $\alpha$ -pinene is being displaced from the reagent by each 2 moles of *trans*-2-butene taken up. Hydrolysis of the reaction mixture resulted in the liberation of hydrogen, corresponding roughly to the presence of one boron-hydrogen bond for each mole of  $\alpha$ -pinene displaced from the reagent.

Similarly, the reaction of *trans*-4-methyl-2-pentene with diisopinocampheylborane proceeds quite slowly. Oxidation of the reaction product after 24 hr. yielded a mixture of 4-methyl-2-pentanol, 68%, and 2-methyl-3-pentanol, 32%. This is in marked contrast to the highly selective course of the corresponding reaction of the reagent with *cis*-4-methyl-2-pentene, where a 96 to 4 distribution of 4-methyl-2-pentanol and 2-methyl-3-pentanol is realized.<sup>3</sup>

Gas chromatographic examination of the reaction mixture revealed the presence here also of  $\alpha$ -pinene in an amount corresponding to 1 mole of  $\alpha$ -pinene for each 2 moles of the olefin reacted. This suggested the possibility that each mole of diisopinocampheylborane might react with 2 moles of *trans*-4-methyl-2-pentene. Accordingly, reaction mixtures were prepared in this ratio, and the uptake of two equivalents of olefin per mole of reagent was observed. A modest change in the relative quantities of the two isomeric alcohols produced in the latter experiments was observed.

The results of these experiments are summarized in Table I.

**Reaction of Hindered Olefins with Diisopinocampheylborane.**—Although cyclohexene is a *cis*-olefin, its reaction with dialkylboranes is very slow. For example, its rate of reaction with disiamylborane is only 1% that of cyclopentene.<sup>7,8</sup> Cyclohexene also reacts with diisopinocampheylborane primarily by displacement, with 1 mole of  $\alpha$ -pinene appearing for each 2 moles of cyclohexene reacting.

The reaction of 2-methyl-2-butene with the reagent is even slower, being only 73% complete in 60 hr. at 0°. Moreover, in this case the  $\alpha$ -pinene displaced amounts to nearly 1 mole per mole of 2-methyl-2-butene taken up. Oxidation of the product from (+)-

(1) Postdoctorate research associate, 1961–1963, on grants (G-6273 and G-19878) provided by the National Science Foundation.

(2) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 486 (1961).

(3) H. C. Brown, N. R. Ayyangar, and G. Zweifel, *ibid.*, **86**, 397 (1964).

(4) H. C. Brown, N. R. Ayyangar, and G. Zweifel, *ibid.*, **84**, 4341 (1962).

(5) G. Zweifel, N. R. Ayyangar, and H. C. Brown, *ibid.*, **84**, 4342 (1962).

(6) P. J. Leroux and H. J. Lucas, *ibid.*, **73**, 41 (1951), report  $[\alpha]_D -13.5^\circ$  for (*-*)-2-butanol.

(7) H. C. Brown and G. Zweifel, *ibid.*, **83**, 1241 (1961).

(8) H. C. Brown and A. W. Moerikofer, *ibid.*, **83**, 3417 (1961).

TABLE I  
 HYDROBORATION OF *trans*-OLEFINS WITH (+)-DIISOPINOCAMPHEYLBORANE<sup>a</sup> IN DIGLYME AT 0°

| <i>trans</i> -Olefin | mmoles | IPC <sub>2</sub> BH <sup>a</sup><br>mmoles | Reaction<br>time,<br>hr. | Olefin<br>reacted,<br>mmoles | Hydrogen<br>evolved on<br>hydrol.,<br>mmoles | $\alpha$ -Pinene<br>displaced,<br>mmoles | Alcohol  |
|----------------------|--------|--|--------------------------|------------------------------|--|--|--|
| 2-Butene             | 50     | 50   | 13                       | 23                           | 31   | 11.6                                     | 2-Butanol  |
|                      | 50     | 50   | 24                       | 50                           | 18   | 24.6                                     | (-)-2-Butanol <sup>b</sup>   |
| 4-Methyl-2-pentene   | 25     | 25   | 24                       | 25                           | 10.8   | 12.0                                     | 68% 4-methyl-2-pentanol <sup>c</sup>   |
|                      |        |  |                          |                              |  |  | 32% 2-methyl-3-pentanol <sup>c</sup>   |
|                      | 50     | 25   | 13                       | 24.1                         | 6.3  | 12.2                                     | 75% 4-methyl-2-pentanol <sup>c</sup>   |
|                      | 50     | 25   | 24                       | 42.5                         | 1.6  | 20.5                                     | 25% 2-methyl-3-pentanol <sup>c</sup><br>78% 4-methyl-2-pentanol <sup>c</sup><br>22% 2-methyl-3-pentanol <sup>c</sup> |

<sup>a</sup> Diisopinocampheylborane, IPC<sub>2</sub>BH, from (-)- $\alpha$ -pinene. <sup>b</sup> Rotation:  $[\alpha]_D^{25} - 1.75^\circ$ . <sup>c</sup> Rotations not determined because of difficulty in separating the two isomeric alcohols on a preparative scale.

 TABLE II  
 HYDROBORATION OF HINDERED OLEFINS WITH (+)- AND (-)-DIISOPINOCAMPHEYLBORANE IN DIGLYME AT 0°

| Olefin                   | mmoles | IPC <sub>2</sub> BH,<br>mmoles | Reacn. time,<br>hr. | Olefin<br>reacted,<br>mmoles | $\alpha$ -Pinene<br>displaced,<br>mmoles | Rotation<br>of alcohol,<br>$[\alpha]_D$ | Optical<br>purity,<br>% |
|--------------------------|--------|--------------------------------|---------------------|------------------------------|--|---|-------------------------|
| Cyclohexene              | 25     | 25 <sup>a</sup>                | 18                  | 21.7                         | 11.4                                     |   |                         |
| 2-Methyl-2-butene        | 100    | 100 <sup>a</sup>               | 60                  | 72                           | 60                                       | -0.75°                                  | 14                      |
| 1-Methylcyclopentene     | 100    | 100 <sup>b</sup>               | 60 <sup>c</sup>     | 66                           | 63                                       | +6.1                                    | 22                      |
| Bicyclo[2.2.2]octan-2-ol | 50     | 50 <sup>a</sup>                | 24                  | 38                           | 34                                       | +6.9 <sup>d</sup>                       | 17                      |

<sup>a</sup> (+)-Diisopinocampheylborane from (-)- $\alpha$ -pinene. <sup>b</sup> (-)-Diisopinocampheylborane from (+)- $\alpha$ -pinene. <sup>c</sup> 25°. <sup>d</sup> From ref. 12.

diisopinocampheylborane produces (-)-3-methyl-2-butanol,  $[\alpha]_D - 0.75^\circ$ , indicating an optical purity of 14%.<sup>9</sup>

Similarly, the reaction of 1-methylcyclopentene with the reagent was only 66% complete in 60 hr. at 25°. Here also 1 mole of  $\alpha$ -pinene was displaced per mole of olefin reacted. The oxidation product from (-)-diisopinocampheylborane proved to be (+)-*trans*-2-methylcyclopentanol,  $[\alpha]_D + 6.1^\circ$ , with an indicated optical purity of 22%.<sup>10,11</sup>

Finally, bicyclo[2.2.2]oct-2-ene also reacts with the liberation of 1 mole of  $\alpha$ -pinene per mole of olefin taken up. In this case the oxidized product, (+)-bicyclo[2.2.2]octan-2-ol (from (+)-diisopinocampheylborane), has a rotation of  $[\alpha]_D + 6.9^\circ$ ,<sup>12</sup> an optical purity of 17%.<sup>13</sup>

The results of these investigations are summarized in Table II.

It was previously demonstrated that the reaction of racemic 3-methylcyclopentene with a deficient amount of diisopinocampheylborane results in a preferred reaction with one of the enantiomers, causing the less reactive isomer to accumulate in the reaction mixture. In this way (+)-diisopinocampheylborane in 50% deficiency produced (-)-3-methylcyclopentene of 45% optical purity.

Application of the same procedure to the relatively sluggish olefin 3-methylcyclohexene resulted in the recovery of (+)-3-methylcyclohexene,  $[\alpha]_D + 4.4^\circ$ .<sup>14</sup> Similarly, hydroboration of 2-methylnorbornene with (+)-diisopinocampheylborane by this procedure resulted in the recovery of (-)-2-methylnorbornene,

(9) P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **97**, 380 (1932), report  $[M]_D + 4.7^\circ$  for 3-methyl-2-butanol.

(10) Based on the value reported for (+)-3-methylcyclopentene (ref. 11), as described later in the paper.

(11) M. Mousseron, R. Richaud, and R. Granger, *Bull. soc. chim. France*, 229 (1946), report  $[\alpha]_D + 77.9^\circ$  for (+)-3-methylcyclopentene.

(12) H. M. Walborsky and A. E. Young, *J. Org. Chem.*, **27**, 2261 (1962).

(13) H. M. Walborsky, M. E. Baum, and A. A. Youssef, *J. Am. Chem. Soc.*, **83**, 988 (1961); J. A. Berson and D. Willner, *ibid.*, **84**, 675 (1962); J. A. Berson and P. Reynolds-Wainhoff, *ibid.*, **84**, 682 (1962); K. Mislow and J. C. Berger, *ibid.*, **84**, 1956 (1962). The authors report  $[\alpha]_D 40^\circ$  for bicyclo[2.2.2]octan-2-ol.

(14) J. H. Brewster, *ibid.*, **81**, 5493 (1959), predicts  $[\alpha]_D + 135^\circ$  for (+)-3-methylcyclohexene.

$[\alpha]_D - 0.73^\circ$ . In both cases the reactions proceed with displacement of  $\alpha$ -pinene.

**Reaction of Hindered Olefins with Triisopinocampheylborane.**—Since the reactions of *trans* and hindered olefins with diisopinocampheylborane are very slow and proceed only with the displacement of  $\alpha$ -pinene from the reagent, it appeared reasonable that the actual hydroborating agent might not be diisopinocampheylborane (or its dimer, *sym*-tetra-isopinocampheylborane<sup>15</sup>), but triisopinocampheylborane formed in a slow dissociation of the parent compound.<sup>16</sup> It appeared possible that the direct formation of triisopinocampheylborane, by the addition of 3 moles of  $\alpha$ -pinene to 2 moles of borane in tetrahydrofuran solution at 0°, would avoid the long reaction times observed in these reactions with hindered olefins while achieving the same results.

This deduction was confirmed. The reaction of 2-methyl-2-butene with triisopinocampheylborane was complete in 3 hr. at 0°, instead of the 60 hr. required for the corresponding reaction with diisopinocampheylborane. The observed rotation of the alcohol product, (-)-3-methyl-2-butanol, was  $-0.91^\circ$ , as compared to  $-0.75^\circ$  observed previously.

Similarly, the reaction of 1-methylcyclopentene was complete in 3 hr. at 0°, in contrast to the 60 hr. at 25°

 TABLE III  
 HYDROBORATION OF HINDERED OLEFINS WITH DIISOPINOCAMPHEYLBORANE AND TRIISOPINOCAMPHEYLBORANE AT 0°

| Olefin               | Reagent <sup>a,b</sup>                                      | Reacn. time,<br>hr. | Rotation<br>of alcohol,<br>$[\alpha]_D$ | Optical<br>purity,<br>% |
|----------------------|---|---------------------|---|-------------------------|
| 2-Methyl-2-butene    | IPC <sub>2</sub> BH <sup>d</sup>                            | 60                  | -0.75°                                  | 14                      |
|                      | IPC <sub>3</sub> B <sub>2</sub> H <sub>3</sub> <sup>d</sup> | 3                   | -0.91                                   | 17                      |
| 1-Methylcyclopentene | IPC <sub>2</sub> BH <sup>c</sup>                            | 60 <sup>c</sup>     | +6.1                                    | 22                      |
|                      | IPC <sub>3</sub> B <sub>2</sub> H <sub>3</sub> <sup>d</sup> | 3                   | -4.8                                    | 17.5                    |
| 1-Methylcyclohexene  | IPC <sub>3</sub> B <sub>2</sub> H <sub>3</sub> <sup>d</sup> | 4                   | -6.9                                    | 18                      |

<sup>a</sup> Diisopinocampheylborane (IPC<sub>2</sub>BH) in diglyme at 0°  
<sup>b</sup> Triisopinocampheylborane (IPC<sub>3</sub>B<sub>2</sub>H<sub>3</sub>) in tetrahydrofuran at 0°. <sup>c</sup> At 25°. <sup>d</sup> Reagent prepared from (-)- $\alpha$ -pinene.

<sup>e</sup> Reagent prepared from (+)- $\alpha$ -pinene.

(15) H. C. Brown and G. J. Klender, *Inorg. Chem.*, **1**, 204 (1962).

(16) H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **84**, 1478 (1962).

TABLE IV  
HYDROBORATION OF REPRESENTATIVE OLEFINS WITH OPTICALLY ACTIVE DIISOPINOCAMPHEYLBORANE AND TRIISOPINOCAMPHEYL-DIBORANE

| Olefin                                      | Reagent <sup>a</sup> | [ $\alpha$ ] <sub>D</sub> |        | Optical purity, % | Displ. of $\alpha$ -pinene | Absolute configuration |                        |  |  |
|---|----------------------|---------------------------|--------|-------------------|----------------------------|------------------------|------------------------|--|--|
|   |                      | Alcohol                   | Olefin |                   |                            | Alcohol                |                        | Olefin                                 |  |
|   |                      |                           |        |                   |                            | Predicted              | Obsd.                  | Predicted                              | Obsd.                                  |
| <i>cis</i> -2-Butene <sup>b</sup>           | D                    | -11.8°                    |        | 87                | No                         | R                      | R                      |  |  |
| <i>cis</i> -2-Pentene <sup>b</sup>          | D                    | - 8.6                     |        | 82                | No                         | R                      | R                      |  |  |
| <i>cis</i> -3-Hexene <sup>b</sup>           | D                    | - 6.5                     |        | 91                | No                         | R                      | R                      |  |  |
| <i>cis</i> -4-Methyl-2-pentene <sup>b</sup> | D                    | -16.0                     |        | 76                | No                         | R                      | R                      |  |  |
| 3-Methylcyclopentene <sup>b</sup>           | D                    |                           | +34.6  | 45                | No                         |                        |                        | R                                      | R                                      |
| 3-Ethylcyclopentene <sup>b</sup>            | D                    |                           | +45.2  | 37                | No                         |                        |                        | R                                      | R                                      |
| Norbornene <sup>b</sup>                     | D                    | - 2.0                     |        | 70                | No                         | 1 <i>S</i> :2 <i>S</i> | 1 <i>S</i> :2 <i>S</i> |  |  |
| Norbornadiene <sup>c</sup>                  | D                    | + 5.8                     |        | 50                | No                         | 1 <i>R</i> :2 <i>S</i> | 1 <i>R</i> :2 <i>S</i> |  |  |
| 1-Methylnorbornene <sup>b</sup>             | D                    |                           | + 6.5  |                   | No                         |                        |                        | (1 <i>S</i> :4 <i>R</i> ) <sup>f</sup> | (1 <i>S</i> :4 <i>R</i> ) <sup>f</sup> |
| <i>trans</i> -2-Butene                      | D                    | + 1.44                    |        | 13                | Yes                        | R                      | S                      |  |  |
| 2-Methyl-2-butene                           | D                    | + 0.75                    |        | 14                | Yes                        | R                      | S                      |  |  |
| 2-Methyl-2-butene                           | T                    | + 0.91                    |        | 17                |                            | R                      | S                      |  |  |
| 1-Methylcyclopentene                        | D                    | + 6.1                     |        | 22                | Yes                        | 1 <i>R</i> :2 <i>R</i> | 1 <i>S</i> :2 <i>S</i> |  |  |
| 1-Methylcyclopentene                        | T                    | + 4.8                     |        | 17.5              |                            | 1 <i>R</i> :2 <i>R</i> | 1 <i>S</i> :2 <i>S</i> |  |  |
| 1-Methylcyclohexene                         | T                    | + 6.9                     |        | 18                |                            | 1 <i>R</i> :2 <i>R</i> | 1 <i>S</i> :2 <i>S</i> |  |  |
| 3-Methylcyclohexene                         | D                    |                           | - 4.4  | (3) <sup>g</sup>  | Yes                        |                        |                        | R                                      | S                                      |
| 2-Methylnorbornene                          | D                    | + 0.73                    |        |                   | Yes                        |                        |                        |  |  |
| Bicyclo[2.2.2]oct-2-ene <sup>d</sup>        | D                    | - 6.9                     |        | 17                | Yes                        | 2 <i>S</i>             | 2 <i>R</i>             |  |  |

<sup>a</sup> To minimize confusion all rotations and configurations are referred to reagents prepared from (+)- $\alpha$ -pinene. D = diisopinocampheylborane; T = triisopinocampheylborane. <sup>b</sup> Ref. 3. <sup>c</sup> K. Mislow and J. G. Berger, *J. Am. Chem. Soc.*, **84**, 1956 (1962). <sup>d</sup> Ref. 12. <sup>e</sup> Ref. 14. <sup>f</sup> Based on reasonable argument, ref. 3.

previously required for only 66% reaction. Again the rotations of the alcohols were comparable.

Finally, we were encouraged to apply the reagent to 1-methylcyclohexene, an olefin which is so sluggish in its reactions with dialkylboranes<sup>8</sup> that we had not attempted previously its utilization in this synthesis. Again the reaction proceeded at a reasonable pace, being essentially complete in 4 hr. Oxidation produced *trans*-2-methylcyclohexanol, [ $\alpha$ ]<sub>D</sub> -6.9°, indicating an optical purity of 18%.<sup>17</sup>

The results are summarized in Table III.

**Absolute Configuration of (-)-*trans*-2-Methylcyclopentanol.**—Although the absolute configurations of the products obtained with both reagents did not correspond to those predicted from the model which had proved so successful for the *cis*-olefins,<sup>3,5</sup> an examination of the data revealed a regularity which suggested that the reaction might still be useful as an empirical tool for configurational assignments. To test this conclusion, it was desirable to establish the absolute configuration of (-)-*trans*-2-methylcyclopentanol in order to ascertain whether its configuration agreed with prediction.

The reaction product, (-)-*trans*-2-methylcyclopentanol, [ $\alpha$ ]<sub>D</sub><sup>20</sup> -4.8°, was converted by standard procedures into the corresponding *p*-toluenesulfonate ester, and the latter heated with sodium isoamylate in diglyme solution to bring about a bimolecular *trans* elimination.<sup>18</sup> The (+)-3-methylcyclopentene formed exhibited [ $\alpha$ ]<sub>D</sub><sup>25</sup> +15.2°, indicating an optical purity of 17.5%.<sup>11</sup> Consequently, the observed rotation for (-)-*trans*-2-methylcyclopentanol corresponds to a 17.5% optical purity, and the calculated maximum rotation for this alcohol is [ $\alpha$ ]<sub>D</sub> -28°. Since (+)-3-methylcyclopentene has the *R*-configuration,<sup>3,4</sup> the (-)-*trans*-2-methylcyclopentanol must have the (1*R*:2*R*)-configuration.

### Discussion

In order to facilitate the discussion, the available experimental results on the reaction of olefins with optically active diisopinocampheylborane and triisopinocampheylborane are summarized in Table IV.

(17) J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5483 (1959), reports [ $M$ ]<sub>D</sub><sup>25</sup> +44.2° for (+)-*trans*-2-methylcyclohexanol.

(18) H. C. Brown and G. Zweifel, *ibid.*, **83**, 2544 (1961).

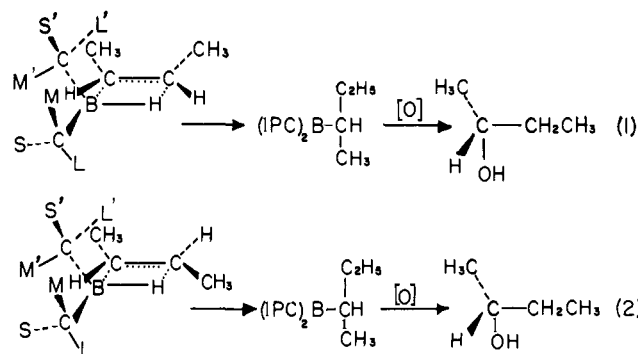
In this summary, to minimize the chances for possible confusion, all of the results have been referred to reagents prepared from (+)- $\alpha$ -pinene.

It is evident that the reactive *cis*-olefins all undergo a rapid reaction with diisopinocampheylborane, without significant displacement of  $\alpha$ -pinene, to produce organoboranes of remarkably high optical purities, in the range of 50 to 90%. Even in the cases where the reagent has been applied for the separation of two enantiomeric olefins, the optical purities of the products are reasonably good.

In the eight cases listed, the absolute configurations of the alcohol or olefin products agree entirely with those predicted from the simple model previously proposed for the steric course of the *cis* addition to diisopinocampheylborane (or its dimer).<sup>3,5</sup>

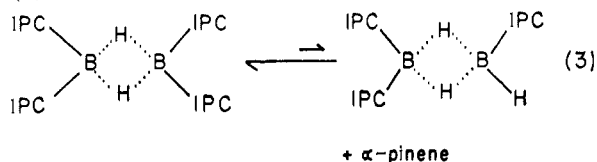
In contrast, the *trans* and hindered olefins react much more slowly with diisopinocampheylborane, and the reactions proceed only with the liberation of  $\alpha$ -pinene from the reagent. Moreover, the optical purities of the products are considerably lower—generally in the range of 13 to 22%. Finally, it is noteworthy that the absolute configurations of the products are not those to be anticipated from the model which serves so well for the reactive *cis*-olefins.

For example, on the basis of the proposed model (1), it would be anticipated that 2-butanol of the same absolute configuration should be formed in the hydroboration-oxidation of the diisopinocampheyl-2-butylborane formed in the addition of either *cis*-(1) or *trans*-2-butene (2) to the reagent.

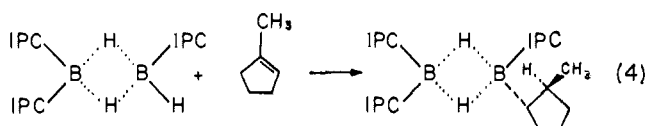


However, the data show that the *trans* and hindered olefins do not undergo a simple addition to the reagent. Consequently, it should not be anticipated that the same simple model would be operable for these displacement reactions.

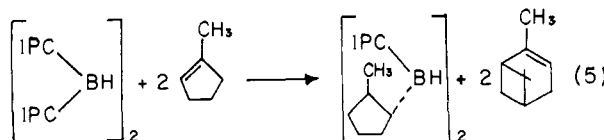
It was previously pointed out that diisopinocampheylborane exists as the dimer, *sym*-tetraisopinocampheylborane, in tetrahydrofuran or diglyme solution and that there was a small measurable dissociation of the reagent into triisopinocampheylborane and  $\alpha$ -pinene (3).<sup>15, 16</sup>



The present results indicate that highly hindered olefins encounter difficulty in achieving a simple addition to the parent molecule, such as is observed with the reactive *cis*-olefins. Consequently, the reaction takes a new path—reaction with the less hindered dissociation product, triisopinocampheylborane (4).

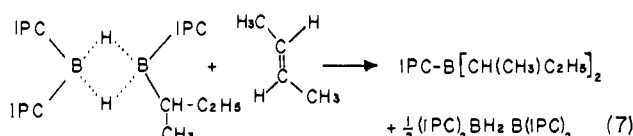
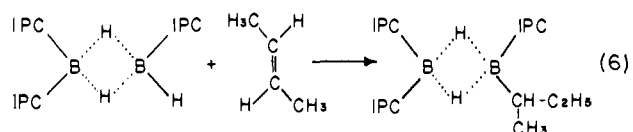


It must be presumed that this product is itself sufficiently hindered that it fails to react directly at any significant rate with a second molecule of the hindered olefin. Instead, a second molecule of  $\alpha$ -pinene is eliminated, and a second mole of the hindered olefin reacts. This process accounts for the one-to-one appearance of  $\alpha$ -pinene for each mole of 1-methylcyclopentene (and other related highly hindered olefins) which is taken up. The over-all stoichiometry of the reaction corresponds, then, to eq. 5.



In this reaction, the slow step is probably the elimination of  $\alpha$ -pinene, first from tetraisopinocampheylborane in the first step, and then from the triisopinocampheylmonoalkyldiborane in the second. This results in a very slow reaction rate, especially in the second stage where the olefin which has added is generally less hindered than  $\alpha$ -pinene, and the reaction product is, therefore, less strained.

In the case of less hindered olefins, such as *trans*-2-butene and cyclohexene, there appears to be no difficulty in adding a second mole to the initial reaction product (6, 7).



This sequence of reactions results in the uptake of 2 moles of olefin per mole of  $\alpha$ -pinene displaced.

Consequently, the interpretations proposed above are consistent with all of the available observations on

the fast reaction of reactive *cis*-olefins with no displacement of  $\alpha$ -pinene, on the slow reaction of *trans* and moderately hindered olefins with 1 mole of  $\alpha$ -pinene displaced per 2 moles of olefin hydroborated, and on the very slow reaction of more hindered olefins with 1 mole of  $\alpha$ -pinene displaced for each mole of olefin reacted.

Further support for the proposed interpretation is provided by the marked difference in directive effects in the hydroboration of *cis*- and *trans*-4-methyl-2-pentene with diisopinocampheylborane. Normally, there is no significant difference in directive effects exhibited in the hydroboration of *cis*-*trans*-olefin pairs by dialkylboranes, such as disiamylborane.<sup>7</sup> However, in the present reaction, the *cis* isomer exhibits the usual marked preference of the boron atom for the less hindered carbon of the double bond (96% 2-, 4% 3-), whereas the *trans* isomer exhibits a much lower discrimination (62% 2-, 38% 3-; Table I). The observed distribution is quite similar to that noted for the hydroboration of *cis*- and *trans*-4-methyl-2-pentene with thexylborane<sup>19</sup> (60% 2-, 40% 3-) and supports the belief that the reaction with the *trans* isomer must proceed through the intermediate formation of triisopinocampheylborane.

By using triisopinocampheylborane in a 1 : 1 mole ratio with the hindered olefin undergoing hydroboration, it is possible to circumvent both the slow first elimination of  $\alpha$ -pinene (3) and the even slower second elimination of  $\alpha$ -pinene from the initial hydroboration product. There does not appear to be any significant difference in the nature of the products realized by the use of triisopinocampheylborane as compared to diisopinocampheylborane.

It was pointed out that the configurations realized in the hydroboration of *trans* and hindered olefins do not correspond to the configurations predicted from the model for a simple addition reaction. However, an examination of the data (Table I) reveals a remarkable consistency in the results—in every case where the configuration of the product is available, the configuration produced is the exact opposite of that predicted for a simple addition to the model.

For example, the 2-butanol from *trans*-2-butene has the *S*-configuration instead of the *R*.<sup>20</sup> 2-Methyl-2-butene produces (*S*)-(+)-3-methyl-2-butanol, instead of the predicted *R*. 1-Methylcyclohexene produces (1*S*:2*S*)-(+)-*trans*-2-methylcyclohexanol instead of the predicted 1*R*:2*R*. Moreover, in the case of bicyclo[2.2.2]oct-2-ene, the bicyclo[2.2.2]octan-2-ol has the 2*R*-configuration, where the model predicts 2*S*.

This consistency in results suggests that the reaction of *trans* or hindered olefins with diisopinocampheylborane (by displacement) or with triisopinocampheylborane (by addition) may provide a highly convenient empirical tool for establishing configurations of products obtainable *via* hydroboration. Accordingly, we wish to propose the following generalization. *Whenever displacement of  $\alpha$ -pinene occurs in stoichiometric amounts in the hydroboration of olefins with diisopinocampheylborane, the alcohol or the olefin obtained will possess the configuration opposite to that predicted on the basis of the simple addition model. For such olefins the use of triisopinocampheylborane will yield the same result.*

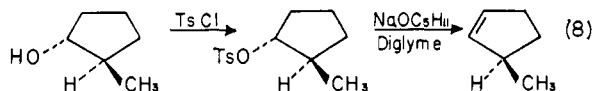
We tested the predictability of this result with *trans*-2-methylcyclopentanol. This alcohol was obtained from 1-methylcyclopentene *via* both diisopinocampheylborane and triisopinocampheylborane. The

(19) G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.*, **85**, 2066 (1963)

(20) For the *R*-*S* configurational nomenclature, see R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

above generalization predicted that the (+) alcohol [from reagent prepared with (+)- $\alpha$ -pinene] should have the 1*S*:2*S* configuration, and the (-) alcohol [from (-)- $\alpha$ -pinene] should have the 1*R*:2*R* configuration.

Accordingly, (-)-*trans*-2-methylcyclopentanol,  $[\alpha]_D -4.8^\circ$ , was converted into the tosylate, and the latter was treated with sodium isoamylate under conditions favorable for the *trans* bimolecular elimination<sup>18</sup> (8).



The observed rotation of the product,  $[\alpha]^{25}_D +15.2^\circ$ , corresponds to the formation of the *R*-configuration for the olefin and this requires the (1*R*:2*R*)-configuration for (-)-*trans*-2-methylcyclopentanol, in agreement with prediction.

It would, of course, be highly desirable to develop a model which would permit the direct prediction of the absolute configuration for the products from triisopinocampheylborane (or by displacement from diisopinocampheylborane). Unfortunately, we have not been successful in developing such a model. It is evident that the problem is considerably more complex than the related reaction involving addition of the reactive *cis*-olefin to diisopinocampheylborane (or its dimer). First, it is apparent that there must be at least two different reaction paths of not very different energies in order to account for the modest optical purities realized. Second, in the unsymmetrical, less crowded structure of triisopinocampheylborane there may well be more than one rotational isomer which could be participating in the reaction. Third, the problem is complicated further by the presence of both terminal and bridge hydrogens—it cannot be stated with any certainty whether the reaction involves one, or the other, or whether the reaction proceeds through competing paths involving both.

In spite of the absence of a satisfactory theoretical basis for the proposed generalization, the observation that it has given consistent results in eight systems of quite different structures lends confidence that it should prove both helpful and reliable, even on an empirical basis.

In conclusion, it appears that both diisopinocampheylborane and triisopinocampheylborane offer promise as a means of converting *trans* and hindered olefins into products of moderate activity ( $\sim 13$  to 22%), and for the establishment of the absolute configurations of such products.

### Experimental

**Materials.**—Diglyme, tetrahydrofuran, and boron trifluoride etherate were purified as described earlier. The physical constants of the hydrocarbons used are given in Table V. The

TABLE V  
SUMMARY OF DATA FOR THE HYDROCARBONS UTILIZED

| Hydrocarbon                        | B.p., °C. | $n^{20}_D$ | Purity, % |
|------------------------------------|-----------|------------|-----------|
| <i>trans</i> -2-Butene             |           |            | 99        |
| 2-Methyl-2-butene                  |           | 1.3890     | 99        |
| <i>trans</i> -4-Methyl-2-pentene   |           | 1.3891     | 99        |
| 1-Methylcyclopentene               | 75–76     | 1.4326     |           |
| 1-Methylcyclohexene                | 108       | 1.4508     |           |
| 2-Methylnorbornene                 | 118       | 1.4620     | 97        |
| (+)- $\alpha$ -Pinene <sup>a</sup> |           | 1.4660     | 99        |
| (-)- $\alpha$ -Pinene <sup>b</sup> |           | 1.4660     | 99        |

<sup>a</sup>  $[\alpha]_D +47.6^\circ$ . <sup>b</sup>  $[\alpha]_D -47.9^\circ$ .

(+)- $\alpha$ -pinene ( $[\alpha]_D +47.6^\circ$ ) and (-)- $\alpha$ -pinene ( $[\alpha]_D -47.9^\circ$ ) were samples made available by Dr. R. A. Bankert, of the Hercules Powder Co., Wilmington, Del., and Dr. J. P. Bain, of the Glidden Co., Jacksonville, Fla. The 2-methylnorbornene was

a sample generously provided by Professor Paul Schleyer of Princeton University.

**Hydroboration of Olefins with Diisopinocampheylborane.**  
**Preparation of Diisopinocampheylborane.**—In a three-necked flask, equipped with a thermometer, condenser, pressure equalizing funnel, and a side arm capped with a rubber septum to permit removal of material, was placed 0.10 mole of (+) or (-)- $\alpha$ -pinene (13.6 g.) in 25 ml. of diglyme, and 37.5 ml. of a 1 *M* solution of sodium borohydride in diglyme. The flask was immersed in an ice bath. Diborane was generated by adding 6.3 ml. of boron trifluoride etherate (50 mmoles) diluted with 15 ml. of diglyme to the well-stirred reaction mixture. During the boron trifluoride addition, the diisopinocampheylborane precipitates. The reagent was maintained for an additional 4 hr. at 0° prior to its use. In cases where ether interferes with gas chromatographic analysis for olefins, the boron trifluoride etherate is replaced by boron trifluoride diglymate.<sup>7</sup>

***trans*-2-Butene.**—To a suspension of (+)-diisopinocampheylborane (50 mmoles) in diglyme was added 3.05 g. of *trans*-2-butene (55 mmoles). The flask was equipped with a cold trap to minimize the loss of olefin. The mixture was stirred for 13 hr. at 0°. Water was then added to decompose residual hydride. The hydrogen evolved was collected. Gas chromatographic analysis indicated that 23 mmoles of *trans*-2-butene had reacted. The organoborane was oxidized with alkaline hydrogen peroxide (16 ml. of 3 *N* sodium hydroxide and 16 ml. of 30% hydrogen peroxide). The mixture was extracted with ether. Gas chromatographic analysis of the ether extract revealed the presence of 16.6 mmoles of  $\alpha$ -pinene.

Hydroboration of *trans*-2-butene (55 mmoles) with the reagent (50 mmoles) for 24 hr. at 0° proceeded to completion. The organoborane was oxidized in the usual way, and the mixture was extracted with ether. Gas chromatographic analysis of the dried ether extract revealed 24.6 mmoles of  $\alpha$ -pinene. The solvent was removed and the residue was distilled. There was obtained (-)-2-butanol,  $[\alpha]^{25}_D -1.75^\circ$ , indicating a 13% optical purity.<sup>6</sup> The results are summarized in Table I.

***trans*-4-Methyl-2-pentene.**—Under identical experimental conditions as described above, *trans*-4-methyl-2-pentene was hydroborated with (+)-diisopinocampheylborane. The organoborane was oxidized with alkaline hydrogen peroxide. The mixture was extracted with ether, and the dried ether extract was analyzed by gas chromatography for  $\alpha$ -pinene, 4-methyl-2-pentanol, and 2-methyl-3-pentanol. The results of these investigations are summarized in Table I.

**1-Methylcyclopentene.**—To a suspension of (-)-diisopinocampheylborane (0.10 mole) in diglyme was added 8.2 g. of 1-methylcyclopentene (0.10 mole) at 0°. The mixture was kept for 2 hr. at 0°, then for 60 hr. at 25°. Water was then added to destroy residual hydride. The organoborane was oxidized at 30–40° by adding 32 ml. of 3 *N* sodium hydroxide, followed by dropwise addition of 32 ml. of 30% hydrogen peroxide. The alcohols formed were extracted with ether, and the ether extract was washed thoroughly with ice water to remove diglyme. Gas chromatographic analysis of the ether extract revealed 63 mmoles of  $\alpha$ -pinene. The ether was removed and the residue distilled. The *trans*-2-methylcyclopentanol (b.p. 142–143°) obtained was contaminated with  $\alpha$ -pinene. Purification of the mixture by gas chromatography gave pure *trans*-2-methylcyclopentanol,  $n^{20}_D 1.4505$ ,  $[\alpha]^{25}_D +6.1^\circ$ , a purity of 22% on the basis of the estimated rotation of the pure isomer arrived at in this study.

**2-Methyl-2-butene.**—Hydroboration of 2-methyl-2-butene (0.10 mole) with (-)-diisopinocampheylborane for 60 hr. at 0° gave after oxidation of the organoborane (-)-3-methyl-2-butanol,  $[\alpha]^{25}_D -0.75^\circ$ , indicating a 14% optical purity.<sup>9</sup>

**Bicyclo[2.2.2]oct-2-ene.**—To a suspension of (+)-diisopinocampheylborane (50 mmoles) in diglyme was added 50 mmoles of bicyclo[2.2.2]oct-2-ene. The mixture was maintained for 24 hr. at 0°, then was hydrolyzed and oxidized. The reaction mixture was extracted with ether. Gas chromatographic analysis of the dried ether extract revealed 12 mmoles of unreacted bicyclo[2.2.2]oct-2-ene and 34 mmoles of  $\alpha$ -pinene. The experimental results are summarized in Table II.

**2-Methylnorbornene.**—To a suspension of (+)-diisopinocampheylborane (50 mmoles) in diglyme was added 10.8 g. of 2-methylnorbornene (100 mmoles). The mixture was stirred for 8 hr. at 0°. Water (1 ml.) was then added to decompose any residual hydride. The unreacted olefin was recovered from the mixture by distillation at room temperature and at reduced pressure (1 mm.). Redistillation gave 4.48 g. of 2-methylnorbornene, b.p. 118° at 753 mm.,  $n^{20}_D 1.4617$ ,  $[\alpha]^{25}_D -0.73^\circ$ .

The remaining organoborane was oxidized in the usual way. The reaction mixture was diluted with *n*-hexane and *m*-xylene, the latter serving as internal standard for  $\alpha$ -pinene. Gas chromatographic analysis indicated 16 mmoles of  $\alpha$ -pinene.

**Hydroboration with Triisopinocampheylborane.**  
**2-Methyl-2-butene.**—In a 200-ml. flask was placed 47 ml. of a 1.06 *M* solution of diborane (50 mmoles) in tetrahydrofuran. The flask was immersed in an ice bath. A 50-ml. solution of (-)- $\alpha$ -pinene (20.4 g., 0.15 mole) in tetrahydrofuran was added to the diborane

solution over a period of 30 min. The reaction flask was permitted to remain for 3 hr. at 0°. The reaction mixture was treated with 3.5 g. of 2-methyl-2-butene (50 mmoles) in 25 ml. of tetrahydrofuran. The flask was maintained for an additional 3 hr. at 0°. Water was then added to decompose residual hydride. The organoborane was oxidized at 30–50° by adding 30 ml. of 3 *N* sodium hydroxide, followed by 21 ml. of 30% hydrogen peroxide. The reaction mixture was then saturated with solid potassium carbonate. The upper phase formed was separated, and the aqueous phase was extracted once more with tetrahydrofuran. The tetrahydrofuran extracts were combined and dried over anhydrous sodium sulfate. The solvent was removed and the 3-methyl-2-butanol was distilled. Purification by gas chromatography gave (–)-3-methyl-2-butanol,  $n_D^{20}$  1.4090,  $d_4^{23}$  0.810,  $[\alpha]_D^{20}$  –0.91°, indicating a 17% optical purity.<sup>9</sup>

**1-Methylcyclopentene.**—Under similar experimental conditions, 100 mmoles of 1-methylcyclopentene (8.2 g.) was hydroborated with 100 mmoles of triisopinocampheylborane derived from (–)- $\alpha$ -pinene. The reaction mixture was maintained for 3 hr. at 0°. Water was then added to decompose residual hydride. The organoborane was oxidized at 30–50° by adding 50 ml. of 3 *N* sodium hydroxide, followed by 42 ml. of 30% hydrogen peroxide. The alcohols formed were worked up in the usual way. Distillation gave 7.62 g. of *trans*-2-methylcyclopentanol

(76% yield), b.p. 58–59° at 12 mm.,  $n_D^{20}$  1.4510,  $d_4^{20}$  0.925,  $[\alpha]_D^{25}$  –4.8°.

The *trans*-2-methylcyclopentanol (5.62 g., 56 mmoles) was dissolved in 20 ml. of pyridine. To this solution was added 61 mmoles of tosyl chloride. The reaction mixture was kept for 12 hr. at 4°, then was poured into a mixture of equal volumes of 6 *M* hydrochloric acid and ether. The upper phase was separated, and the aqueous phase extracted with ether. The combined ether extracts were washed with water, and dried. Evaporation of the ether gave 14 g. of crude tosyl ester.

In a 300-ml. flask was placed 45 ml. of isoamyl alcohol and 45 ml. of diglyme. To this mixture was added sodium hydride until 0.12 mole of hydrogen was evolved. The tosyl ester was added and the reaction mixture was heated until the olefin distilled. There was obtained 3.1 g. of 3-methylcyclopentene, b.p. 66° at 752 mm.,  $n_D^{20}$  1.4210,  $d_4^{25}$  0.760,  $[\alpha]_D^{25}$  +15.2°, indicating a 17.5% optical purity.<sup>11</sup>

**1-Methylcyclohexene.**—Fifty mmoles of 1-methylcyclohexene (4.8 g.) was hydroborated with 50 mmoles of triisopinocampheylborane derived from (–)- $\alpha$ -pinene. The organoborane was oxidized, and the alcohol formed was worked up in the usual way. Purification by gas chromatography gave pure *trans*-2-methylcyclohexanol,  $n_D^{25}$  1.4620,  $d_4^{20}$  0.923,  $[\alpha]_D^{25}$  –6.9°, indicating an 18% optical purity.<sup>17</sup>

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

## Hydroboration. XX. The Reaction of Diisopinocampheylborane with Representative 2-Methyl-1-alkenes—A Convenient Synthesis of Optically Active 2-Methyl-1-alkanols

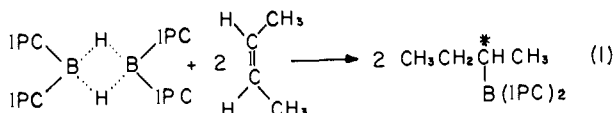
BY GEORGE ZWEIFEL, NAGARAJ R. AYYANGAR,<sup>1</sup> TAKASHI MUNEKATA,<sup>2</sup> AND HERBERT C. BROWN

RECEIVED OCTOBER 3, 1963

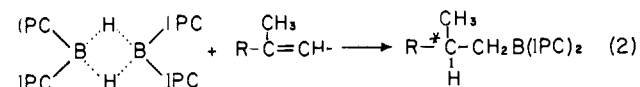
(+)-Diisopinocampheylborane readily adds to 2-methyl-1-butene, 2,3-dimethyl-1-butene, and 2-phenylpropene to produce new organoboranes containing a new asymmetric center at the 2-position. Oxidation produces optically active alcohols, all of the *R*-configuration: (+)-2-methyl-1-butanol,  $[\alpha]_D +1.25^\circ$ , 21% optical purity; (–)-2,3-dimethyl-1-butanol,  $[\alpha]_D -1.88^\circ$ , 30% optical purity; (+)-2-phenyl-1-propanol,  $[\alpha]_D +0.80^\circ$ , 5% optical purity. On the other hand, the reaction of 2,3,3-trimethyl-1-butene is slow and proceeds with displacement of  $\alpha$ -pinene from the reagent. The oxidized product, 2,3,3-trimethyl-1-butanol, exhibits  $[\alpha]_D -5.1^\circ$ , of unknown absolute configuration. The model previously proposed to account for the related reaction of reactive *cis*-olefins has been adapted to permit prediction of the absolute configuration of alcohols and related products realized through the simple addition of such terminal olefins to (+)- and (–)-diisopinocampheylborane.

The success realized in achieving asymmetric syntheses through the reaction of (+)- and (–)-diisopinocampheylborane with *cis*-olefins<sup>3,4</sup> and of triisopinocampheylborane with *trans* and hindered olefins<sup>5</sup> led us to explore the possible extension of this asymmetric synthesis to some representative terminal olefins.

In the case of the internal olefins previously explored,<sup>4,5</sup> the boron becomes attached to the asymmetric center (1).



In the case of the 2-methyl-1-alkenes examined in the present study, the asymmetric center is on the carbon atom immediately adjacent to that holding the boron atom (2).



Consequently, it was anticipated that the magnitude of the asymmetric induction would be less than that realized for the *cis*-olefins.

(1) Postdoctorate research associate, 1961–1963, on grants (G-6273 and G-19878) provided by the National Science Foundation.

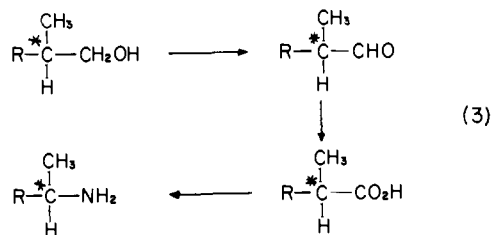
(2) Visiting Scholar, 1962–1963, on funds provided by the Kureha Chemical Industry Co., Tokyo, Japan.

(3) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 486 (1961).

(4) H. C. Brown, N. R. Ayyangar, and G. Zweifel, *ibid.*, **86**, 397 (1964).

(5) H. C. Brown, N. R. Ayyangar, and G. Zweifel, *ibid.*, **86**, 1071 (1964).

In the case of the *cis*-olefins it proved possible to develop a model for the hydroboration stage which permitted the reliable assignment of configuration to eight products of considerably different structures.<sup>4</sup> For such applications it is not important that the products have high optical purities. It is far more important that the method predict reliably the configuration of the initial derivative, so that it can be used to relate the configurations of a family of derived products (3).



Accordingly, we undertook the hydroboration-oxidation of 2-methyl-1-butene, 2,3-dimethyl-1-butene, 2,3,3-trimethyl-1-butene, and 2-phenylpropene in order to examine (a) the practicality of asymmetric syntheses in terminal olefins of this type, and (b) the possibility of developing a model which would predict the absolute configurations of any optically active products thus produced.

### Results

(+)-Diisopinocampheylborane, synthesized from (–)- $\alpha$ -pinene by hydroboration with sodium borohydride and boron trifluoride in diglyme in the usual